UCRL-10215

University of California

Ernest O. Lawrence Radiation Laboratory

Berkeley, California

DISCLAIMER

UCRL-10215

UNIVERSITY OF CALIFORNIA
Lawrence Radiation Laboratory
Berkeley, California

Contract No. W-7405-eng-48

HEALTH PHYSICS ASPECTS OF WHOLE-BODY IRRADIATION

Graham M. Hairr

June 20, 1962

HEALTH PHYSICS ASPECTS OF WHOLE-BODY IRRADIATION

Graham M. Hairr

Lawrence Radiation Laboratory
University of California
Berkeley, California

June 20, 1962

ABSTRACT

Biomedical research personnel at Lawrence Radiation Laboratory, Berkeley, have been developing techniques of lymphatic leukemia therapy by massive doses of yttrium-90 administered intravenously. A desired further application is suppression of the immune mechanism prior to tissue transplant. For assurance of purity the yttrium-90 has been processed at the site from multicurie shipments of strontium-90.

Health Physics problems that had to be resolved are outlined. These include development of shielded and remotely operated Y^{90} extraction equipment; development of equipment for preliminary animal experimentation; and development of carrying containers for intralaboratory movement of curie quantities of beta emitters. The final development problem produced an enclosure to comfortably house a human patient and the associated medical equipment for his treatment, providing adequate shielding for the attending medical team and yet providing for quick access in case of a medical emergency. Control methods were also developed for keeping radioactive contamination from spreading after the patient was transferred to a conventional hospital room which, for medical reasons, had to be pressurized for reverse isolation.

HEALTH PHYSICS ASPECTS OF WHOLE-BODY IRRADIATION*

Graham M. Hairr

Lawrence Radiation Laboratory
University of California
Berkeley, California

June 20, 1962

INTRODUCTION

For the past several years researchers at the Donner Laboratory of Medical Physics, Lawrence Radiation Laboratory, Berkeley, have been developing techniques for successful tissue transplant or leukemia therapy (or both) in large mammals such as dogs, monkeys, and man by delivering high doses of radiation to the tissue responsible for the "immune response" without causing death of the subject from other forms of radiation damage. This paper deals with the health physics aspects of this program for whole-body irradiation using internally administered radioisotopes.

*Work done under the auspices of the U. S. Atomic Energy Commission

RADIOISOTOPE PRODUCTION

Selection of Isotope

Yttrium-90 chelated with DTPA (diethylene triamine penta acetic acid) was the isotope selected by the researchers to deliver high doses of internal radiation. There were four main reasons for this decision:

(a) The chelated yttrium compound permits some degree of selectivity in irradiating the lymphatic cells, which are responsible for the rejection of foreign tissue.

(b) Since yttrium-90 is a pure beta emitter, a high radiation dose to the subject involves only a relatively low dose to the attending medical team.

(c) The short biological half-life of chelated yttrium-90 aids in controlling the total dose and in reducing the dose rate to the attending medical team during procedures following the irradiation.

(d) The radioactive half-life of 64 hours is long enough to permit production by milking from the strontium-90 parent and yet short enough to permit some decontamination by decay.

One of the medical decisions reached in the first stages of the project was that no human subject would be left with more than one-half of one body burden of Sr^{90}. Since Y^{90} of sufficient purity was not available commercially at the time, a chemical separation program had to be set up as a prerequisite to the research.

Y^{90} Separation

Y^{90} is separated from the Sr^{90}-Y^{90} equilibrium mixture by modifications of the method used by Oak Ridge National Laboratory. An organic phosphate (di-2 ethyl-hexyl-phosphoric acid) in toluene solution is used, and steps are taken to minimize the amount of Sr^{90} contamination and to bring the Y^{90} into a convenient soluble form. The flow sheet is shown in Fig. 1.

This "milking" process requires a radioisotope enclosure of about 12 cubic feet volume. Remote tong operation through a 2-inch lead shield is necessary because of bremsstrahlung from the 40 to 50 curies of beta emitter.

The major design considerations in setting up this process were as follows:

(a) Because of the acid fumes involved, nonmetallic materials were used wherever practical and all metal surfaces were covered with an acid-resistant coating (Bisonite).

(b) Each piece of equipment was made remotely replaceable to minimize residual Sr^{90} contamination and glassware discoloration from radiation damage.

(c) All equipment was mounted from above to allow the use of disposable vinyl floor coverings and permit floor storage of the isotope within a lucite shield.

(d) To minimize tong manipulations, the pieces of extraction equipment were located in a 180° arc around a central cone holder which has an electric drive for vertical and horizontal movements.

(e) An acid fume condenser was provided with a condensate flask and a scrounge pipette.

The items that required floor mounting (a heat source, the acid fume condenser, and the condensate flask) were located in the left rear corner. A pass-through port, which can be reached with one tong, was installed in the right rear corner for access to an adjoining Y^{90} enclosure.

Radioactive waste in ice cream cartons is passed out of the left side of the enclosure, by use of tongs, into an enclosed polyethylene bag on a hydraulic passout ring. After a heat seal is made and cut through, the plastic bag is lowered into a 1 1/2-inch lead waste-transfer container, covered, and removed to a waste-packaging area. This bagging and sealing unit is attached to the 2-inch lead cave and shielded with 2 inches of brass.

Figures 2 and 3 show a general view of the Sr^{90} enclosure.

Y^{90} Enclosure

To minimize the risk of recontaminating the Y^{90} with Sr^{90} following the separation, a separate enclosure is provided at right angles to the Sr^{90} enclosure with a pass-through door. This enclosure is divided into a large and a small section by a 1/2-inch-thick lucite wall in which is a tong-operated door. The larger section, which has about two-thirds of the floor area, is used for removal of assay aliquots, addition of the DTPA chelating agent, and preparation of the Y^{90} DTPA for final transfer.

Figure 4 shows a general view of the Y^{90} enclosure.

The smaller section is used for filling the Y^{90} transfer container. This container, a 3-ounce jar, shown in Fig. 5, is placed in the small chamber within its transport shielding and Tube 1 (Fig. 5) is passed through an aperture in the lucite wall into the large compartment, where it is fitted to a 30-cc hydraulic pipette into which the desired quantity of Y^{90} DTPA solution has been drawn for transfer. Line 4 (Fig. 5) is fitted to a syringe; upon withdrawal

of the plunger and simultaneous depression of the hydraulic control on the 30-cc pipette, the Y^{90} DTPA solution is drawn into the jar. Lines 1 and 4 are then heat-sealed and the isotope in its container can be moved to the medical area.

Caustic Scrubber

In addition to the condenser in the Sr^{90} enclosure, a separate caustic scrubber unit within a lead shield is provided for removal of acid fumes from the air exhausted from the entire train of enclosures. This feature was found necessary in the early days of the project when condensed acid, primarily from the aqua regia ashing process, damaged the "absolute" filter in the exhaust system. The caustic scrubber used is a standard type developed by the Health Chemistry Department some years previously for recirculating enclosure atmospheres in heavy-element separation procedures.

Figure 6 shows a general view of the caustic scrubber unit.

Performance

One properly trained operator using this series of enclosures can achieve a high-purity Y^{90} separation of about 75% yield in about 6 hours. The radiation field, mainly from bremsstrahlung, in the operator's area in front of the Sr^{90} cave ranges from about 1 to 3 mr per hour.

Figures 7 and 8 show the Sr^{90}-Y^{90} separation train.

ANIMAL STUDIES

The major technical problem in Y^{90} DTPA animal studies has been contamination control during recirculation of the isotope. This recirculation is necessary because studies of single intravenous injections on mice and dogs have indicated rapid and nearly complete excretion of the chelated Y^{90} via the urine. To achieve a high and accurately measured total body dose the known level of isotope must remain in the body for a prescribed time. To resolve this problem the researchers developed a technique of intravenously recycling the urine for a period of 6 hours.

Figure 9 shows a schematic representation of the urine intravenous recycling system.

Most of the animal experimentation was with pure-bred male beagle dogs 6 months to 2 years old. An animal irradiation cave was provided of 3/4-inch plywood lined with vinyl sheeting with a 3/4-inch-thick lucite viewing front with glove ports. During the recycling period the anesthetized animal is suspended in a vinyl hammock which has holes for his legs. During

typical experiments the radiation field within the enclosure is from 4 to 6 r per hour and outside the enclosure from 2 to 5 mr per hour. At the end of the 6-hour recycling period the animal is removed from the enclosure through a large oval passout ring into a polyethylene bag and moved to a holding cage. The holding cages are now being redesigned to permit additional medical procedures, such as bone marrow transplants, to be done by a team of medical researchers without removing the animal. Investigators from another site are now participating in the program, and additional facilities are being installed to permit washing off skin and fur contamination before the animals are taken home.

Y^{90} DTPA THERAPY IN HUMANS

Equipment

In the fall of 1961 the researchers had achieved apparent success in homologous bone marrow transplantation between unrelated beagle dogs and were ready for the use of Y^{90} DTPA in human patients. The desired result in the human patient is suppression of the immune response, so as to allow the "take" of a bone marrow transplant following irradiation for acute lymphatic leukemia. The amount of activity required to suppress the immune response is about 6 to 10 mC of Y^{90} DTPA per pound of body weight, thus approaching 1.5 C in some cases.

An enclosure for the patient was desired to prevent contamination of the attending medical personnel and the hospital room in case of accident during the irradiation procedure. The main design criteria for this enclosure were as follows:

(a) Reasonable shielding must be provided against the beta activity within.

(b) The enclosure atmosphere must be at a negative pressure relative to the hospital room and exhausted to the outdoors through suitable high-efficiency filters.

(c) Since it is medically advantageous to have the patient not anesthetized, every reasonable provision must be made for the patient's comfort within the enclosure during a period of as much as 24 hours. In particular, the enclosure must be cheerful and light to minimize any possibility of panic or claustrophobia.

(d) The enclosure must be fitted with enough glove ports for the medical personnel to carry out all necessary procedures. The enclosure sides must also be demountable in seconds, however, to permit the physician unrestricted access to the patient in case of any dire medical emergency.

(e) Suitable shelves, apertures, and annex enclosures must be provided for the recycling apparatus and other medical equipment.

(f) Because of limited storage space at the hospital, the enclosure must be an integral mobile unit adapted to rapid installation or removal.

A general view of the human patient enclosure is shown in Fig. 10. This is a rectangular unit 7 feet long, 4 feet high, and 3 feet wide, constructed of 3/4-inch plywood and four side sections of 3/4-inch lucite. The four side sections, and a center support on one side, are removable by simply twisting simple outside clamps 90°.

The patient rests on an ambulance cot which has been modified to provide adjustable arm rests and head and knee sections which are hydraulically adjustable from the outside. The hydraulic fluid lines have Hansen fittings at the cylinder on the cot for immediate disconnection should it be necessary to remove the patient on the cot. Two hand bars are suspended from the ceiling to enable the patient to shift himself. A small intercommunications unit is provided.

Air flow through the enclosure is provided by two blowers mounted underneath and regulated to a maximum of 10 cubic feet per minute. The high-efficiency filters are mounted on top of the enclosure.

Each of the lucite side panels has a rotating center section which in turn contains two rotating 8-inch-diameter glove ports. A pass-in and pass-out aperture is provided at one end of the enclosure to supply the patient with any small items he desires.

Operating Procedures

During the 6-hour period of intravenous urine recycling, continuous monitoring is provided for the protection of the medical personnel. Periodic swipes of the area around the enclosure and of the enclosure itself are taken, combined with intermittent checks of the filter that is sampling the general room air at a rate of 4 cfm. Although the radiation field within the enclosure has ranged from 250 mr per hour to 1 r per hour at 1 1/2 to 2 feet and 10 r per hour at approximately 3 inches from the patient, radiation fields at the outer surfaces of the enclosure have ranged from 0.2 to 2.5 mr per hour and the general background in the hospital room has been 0.2 mr per hour or less.

Figure 11 shows the human irradiation enclosure in use.

Upon completion of the 6-hour recyling procedure the patient remains in the enclosure for an additional 15 to 20 hours, during which the body eliminates some 99% of the remaining activity. During this time urine from

an indwelling catheter is collected beneath the enclosure in polyethylene bottles which are shielded by a mixture of sawdust and plaster of Paris. Radiation from the first five urine collections, which span a 10-hour period, has ranged from 2 r per hour to 150 mr per hour at about 1 foot, not shielded. The top of the polyehtylene bottle is provided with a transflexed tube neck, which can be heat-sealed to permit periodic replacement of full bottles.

Following this additional 15- to 20-hour period the patient is transferred from the enclosure to a conventional hospital bed. Because of the susceptibility of the patient to infection after the irradiation, a "reverse isolation" approach is mandatory. To maintain such an environment the room was pressurized with a high-efficiency filter in the air intake and an internal air conditioner to maintain constant room temperature.

Typical measurements at this time of transfer have shown from 40 mr per hour to 100 mr per hour over the head and neck region, or in other words, radiation less than that emanating from patients who have received the more widely known "iodine cocktail." From this point on, the main emphasis from a health physics point of view is to control as closely as feasible all urine and saliva. For example, all eating utensils are of a disposable type, and all towels and other laundry possibly contaminated are thoroughly monitored and the contaminated items segregated for decay. The researchers have generally acquired 100% body waste collection in order to make a material balance on the isotope.

Experience to date has been that after approximately 4 to 6 weeks no further radioactivity can be detected in the patient, and he may then be considered "cold." During this time, because of the vulnerability of the patient to infection, the number of people entering the room has been held to an absolute minimum. With a nominal amount of training, members of the medical personnel have been able to perform such traditional health physics tasks as changing air samples, bagging waste, taking swipes for surface contamination assessment, and making direct surveys of potentially contaminated equipment. This procedure has proved entirely feasible.

Although at this writing the results of the program from a medical point of view are still too tentative for comment within the scope of this paper, we can state from a health physics viewpoint that the results have shown that curie levels of radioisotope can be administered to human patients by means of these techniques and procedures, with reasonably low radiation exposures to the medical team, and a very slight and wholly acceptable risk of contamination spread to the hospital environment. Although to date

relatively few patients have undergone this treatment in one isolated room of a general student hospital, we feel that the approach taken is quite suitable to more ambitious programs, and fully intend to pursue it if the Donner Laboratory of Medical Physics achieves greater facilities for human patient treatment.

Acknowledgement

I wish to thank Mr. Pat Howe for the opportunity to present this report and Mr. Harvey Soule for his many helpful suggestions and encouragement in its preparation. Much appreciation goes to Mrs. Patricia Allen for her assistance in preparing the manuscript.

Many thanks to Dr. Myron Pollycove, Dr. H. Saul Winchell and Mr. William Laughman for their interest and helpful comments relating to the technical aspects of the work described.

Figure Captions

Fig. 1. Procedure for separation of Y^{90} from Sr^{90}-Y^{90} mixture.

Fig. 2. Sr^{90}-Y^{90} separation enclosure.

Fig. 3. Sr^{90}-Y^{90} separation enclosure.

Fig. 4. Y^{90} enclosure.

Fig. 5. Y^{90} container.

Fig. 6. Scrubber box assembly.

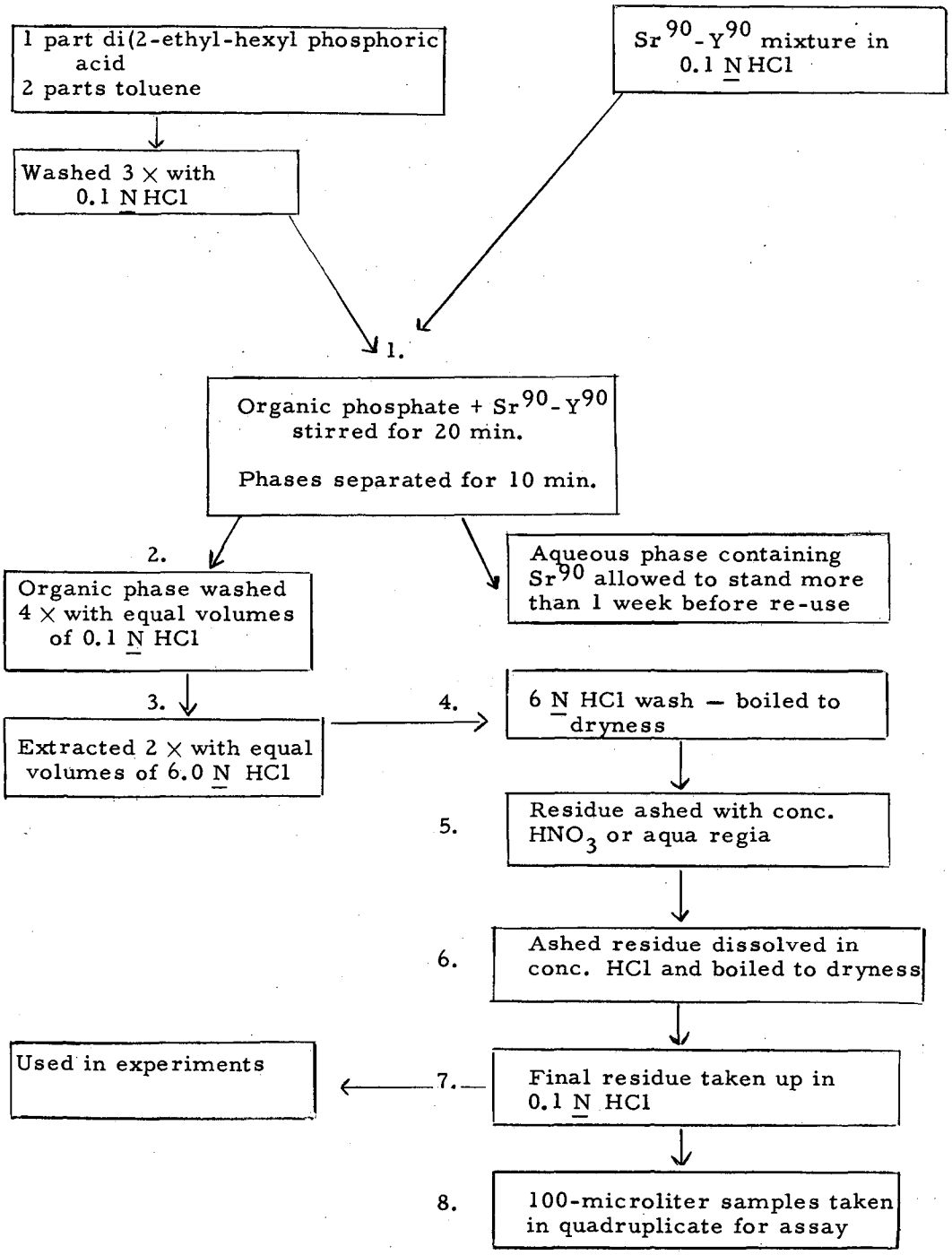
Fig. 7. Sr^{90}-Y^{90} separation train.

Fig. 8. Sr^{90}-Y^{90} shield train.

Fig. 9. Schematic representation of urine intravenous recycling system.

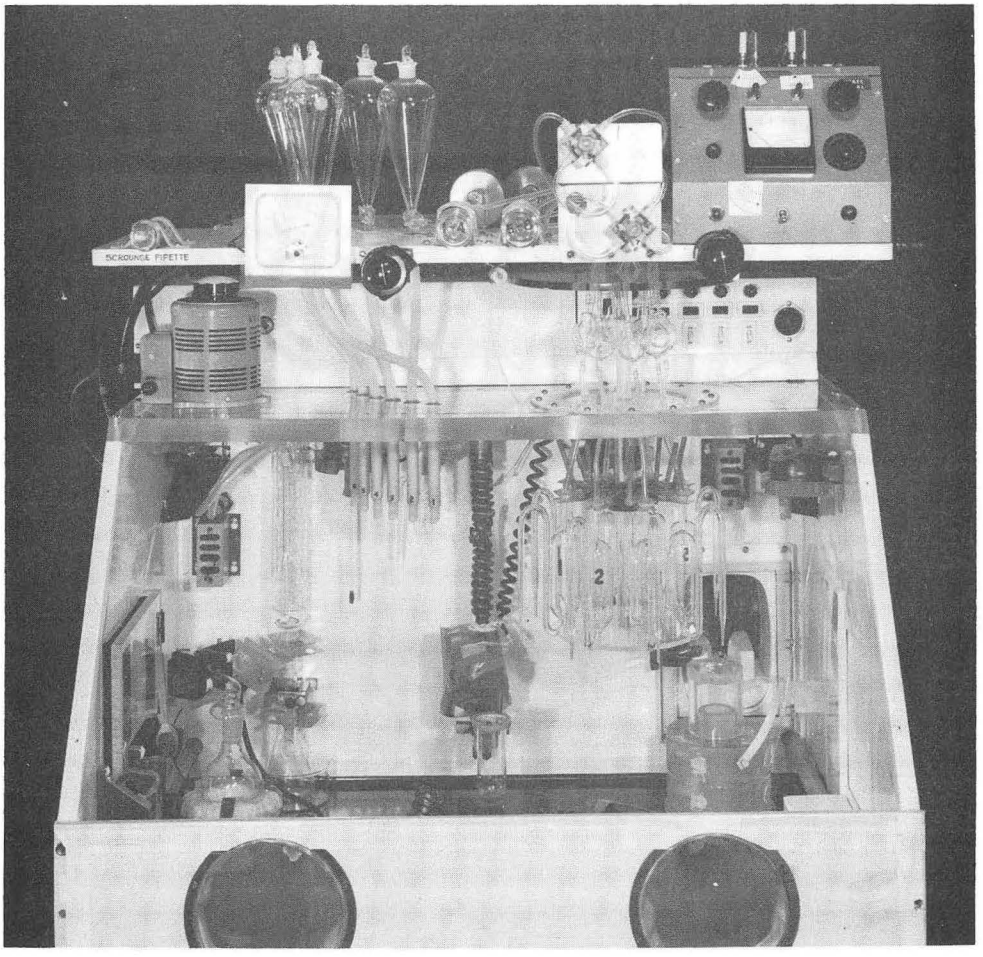
Fig. 10. Human irradiation enclosure.

Fig. 11. Human irradiation enclosure in use.



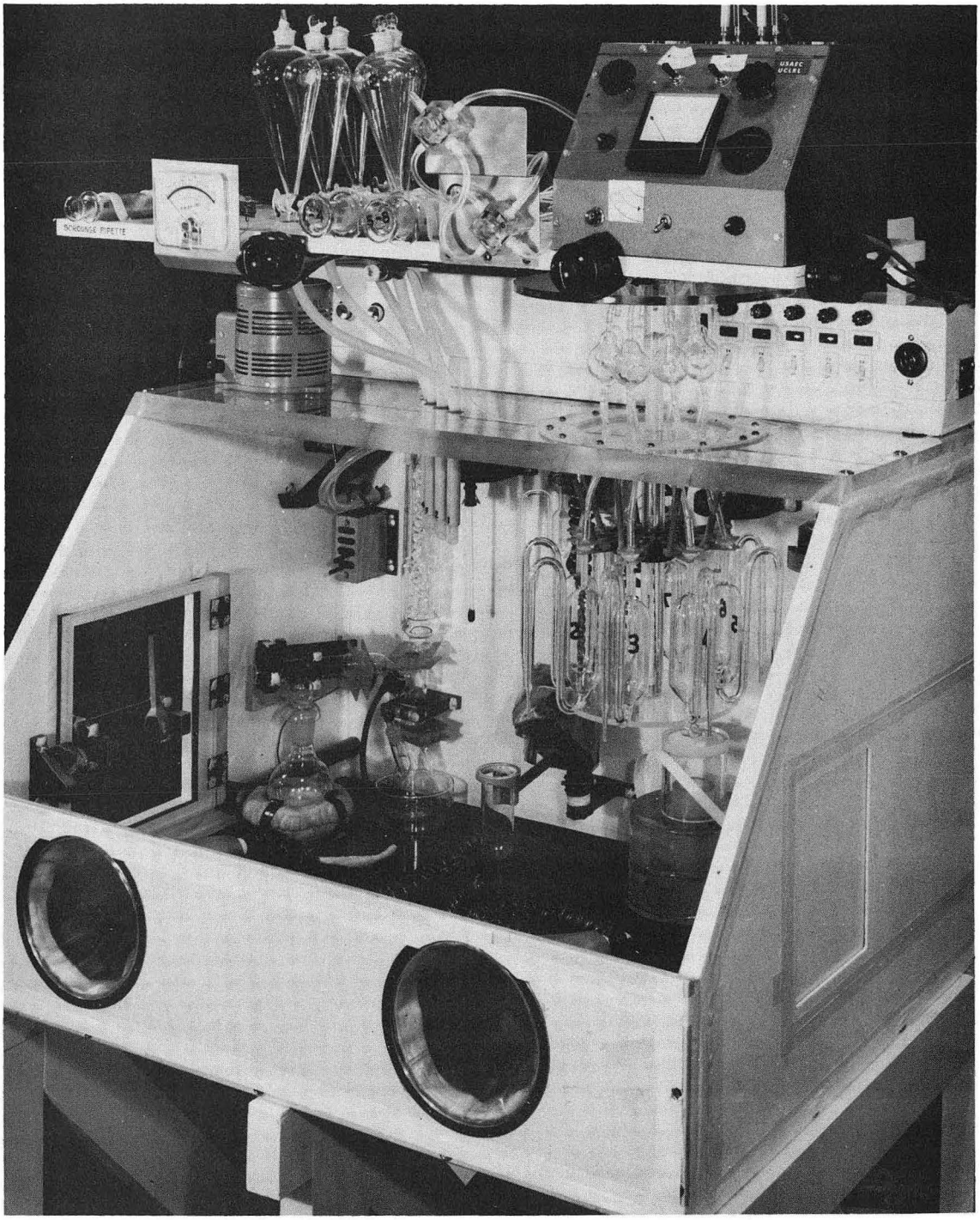
MUB-1222

Fig. 1



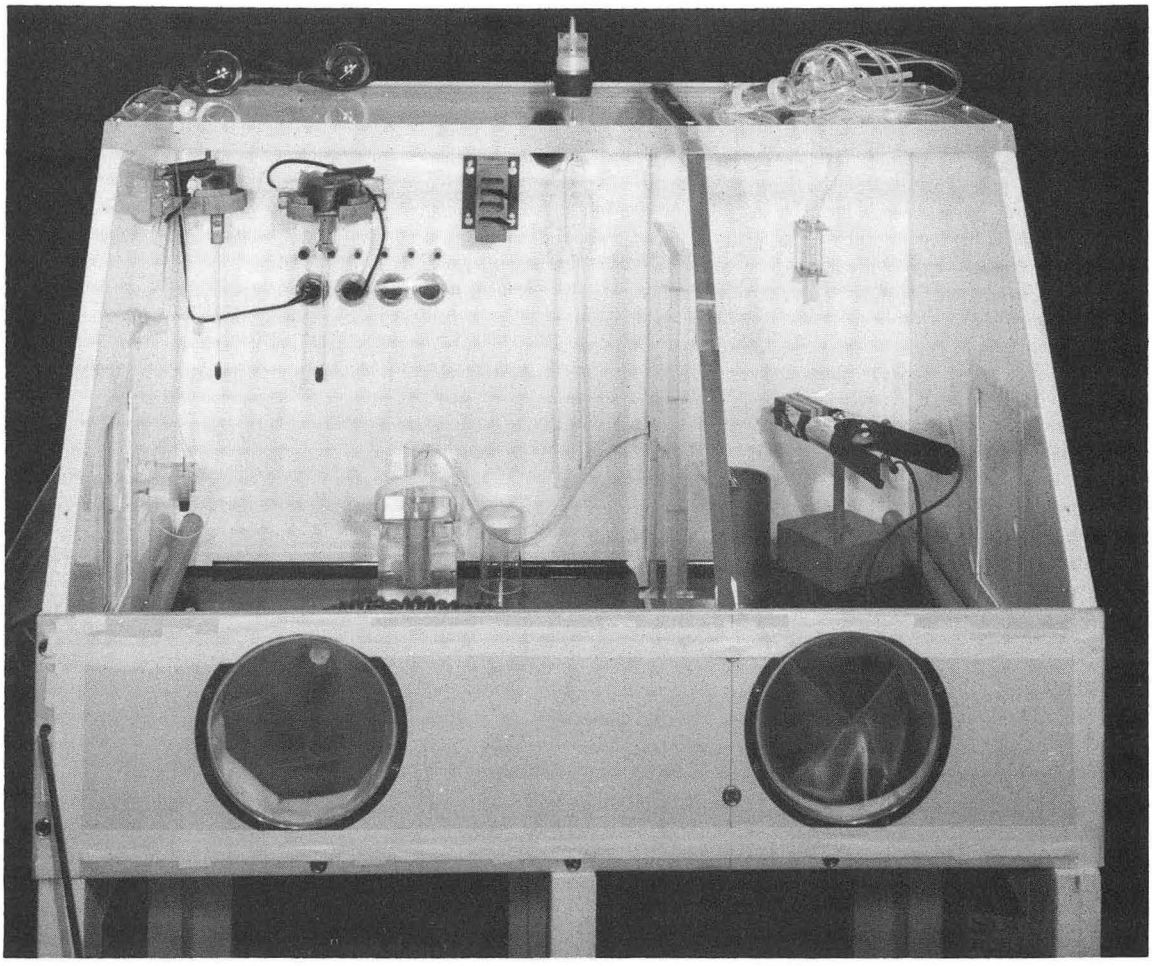
ZN-3140

Fig. 2



ZN-3141

Fig. 3



ZN-3139

Fig. 4

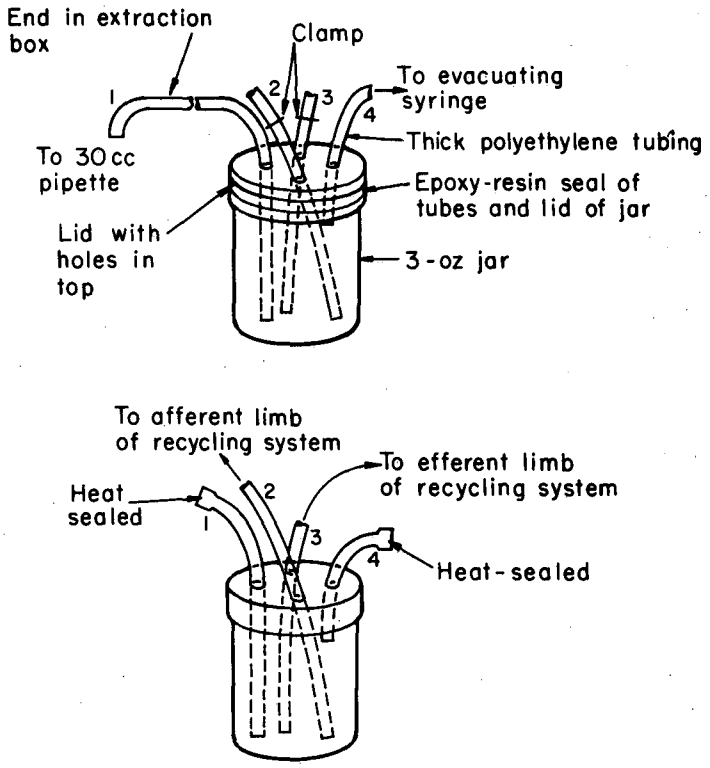
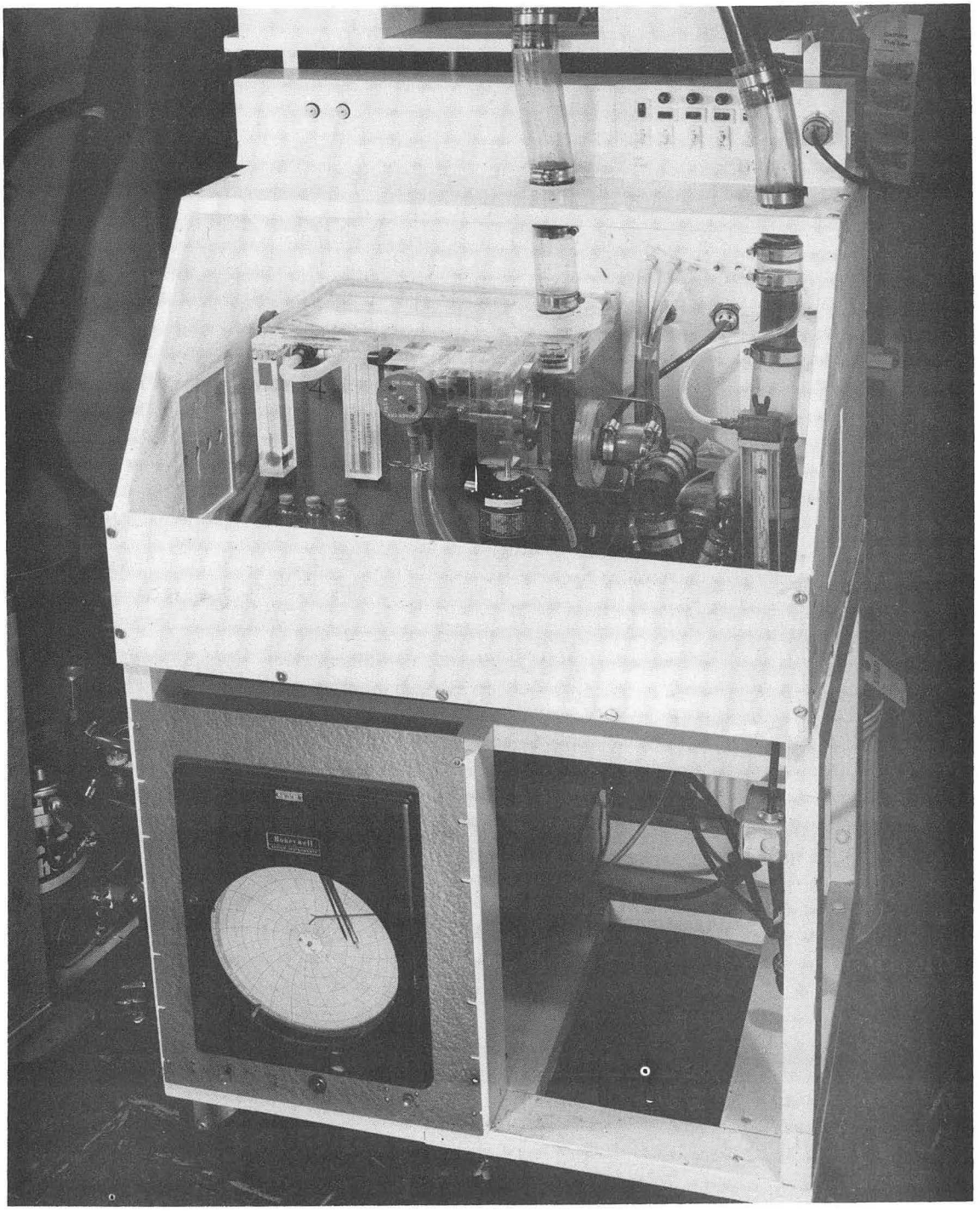
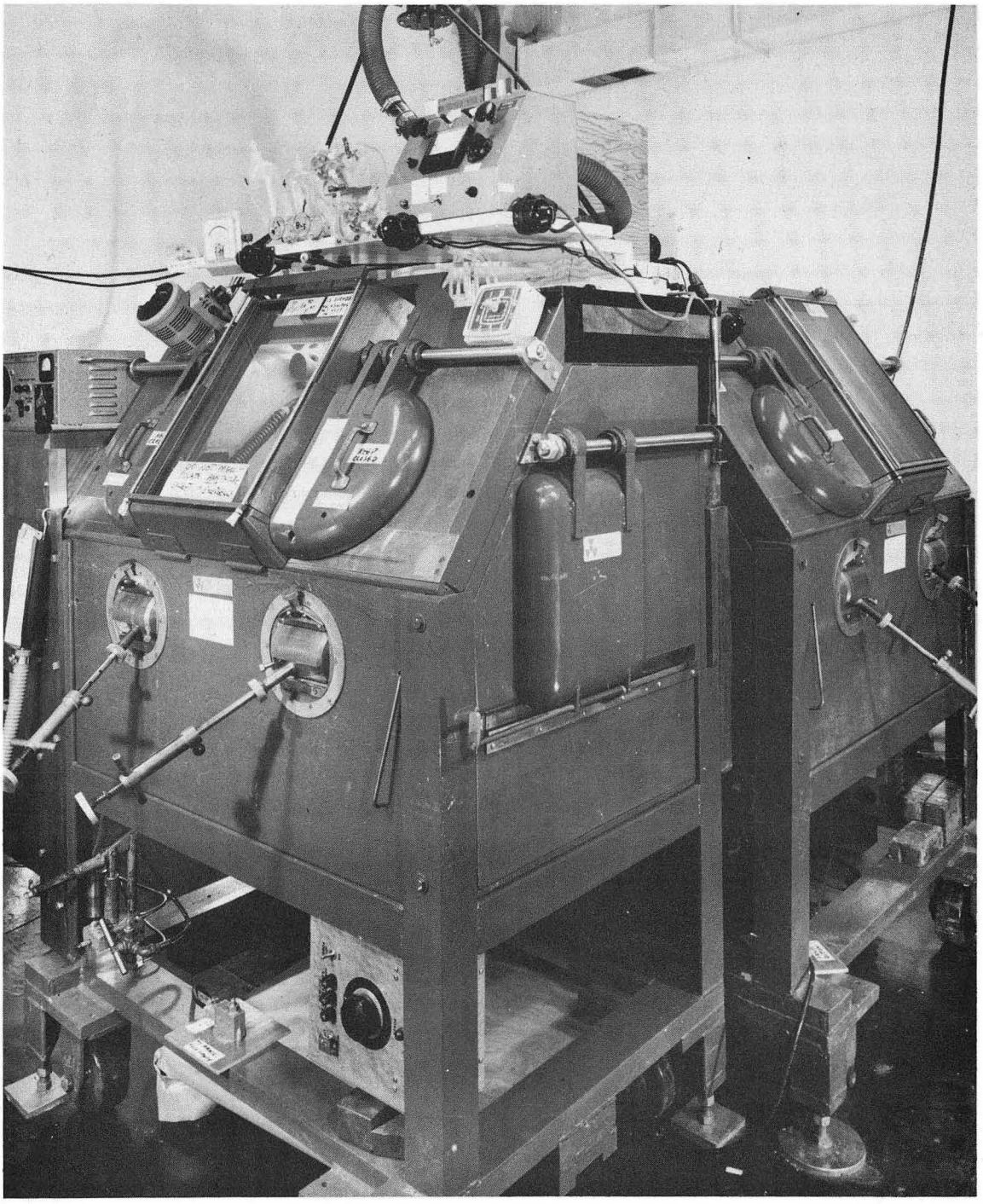

End in extraction box
Clamp
To evacuating syringe
1
2
3
4
Thick polyethylene tubing
To 30 cc pipette
Epoxy-resin seal of tubes and lid of jar
Lid with holes in top
3-oz jar
To afferent limb of recycling system
To efferent limb of recycling system
Heat sealed
Heat-sealed
MU-26833

Fig. 5



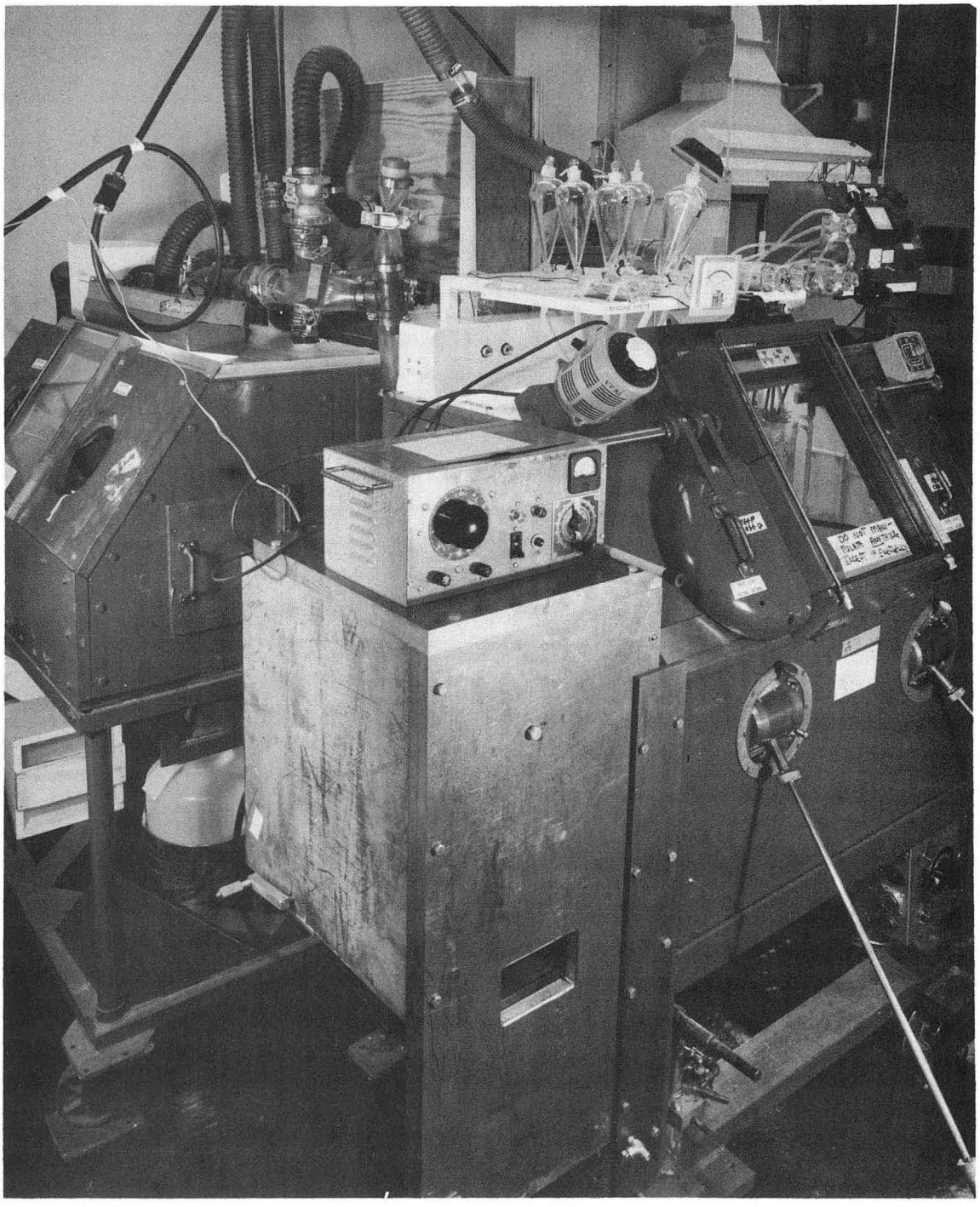
ZN-3138

Fig. 6



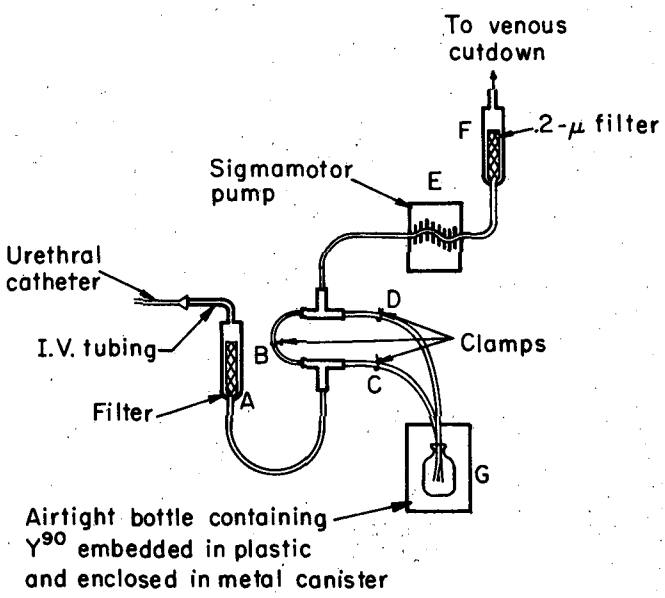
ZN-3142

Fig. 7



ZN-3137

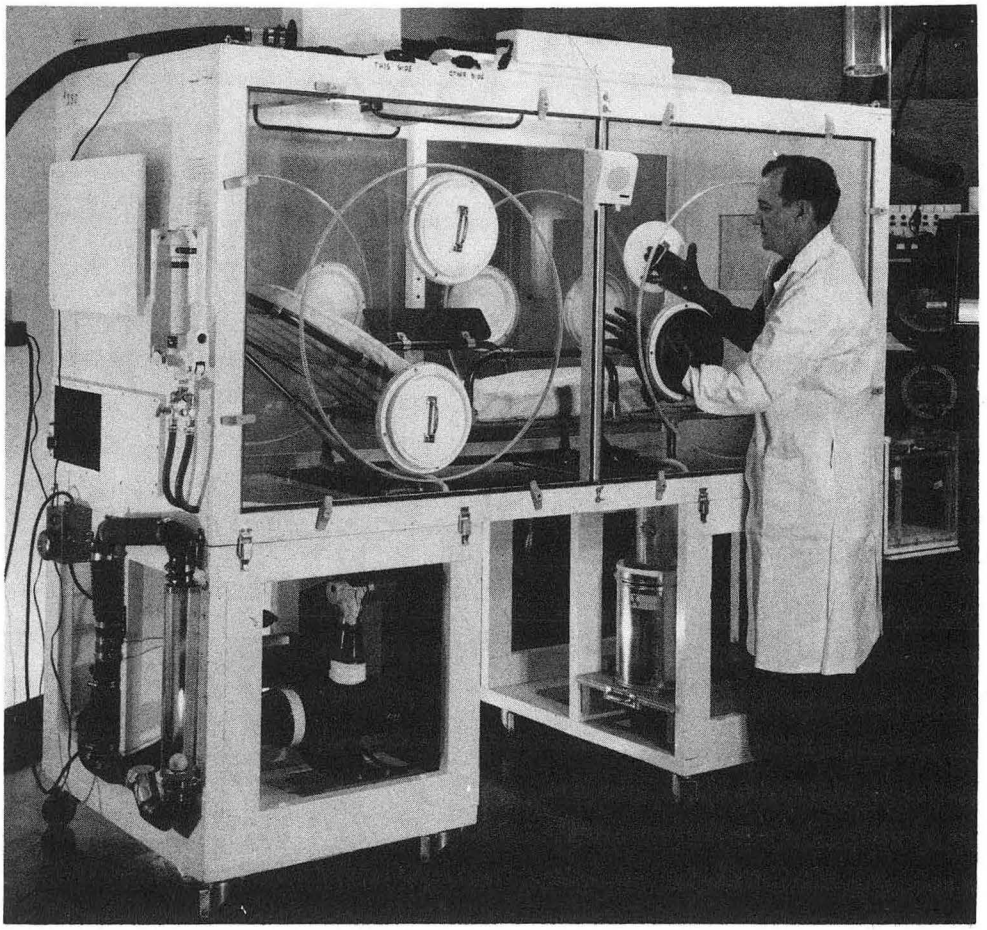
Fig. 8



Schematic representation of urine intravenous recycling system

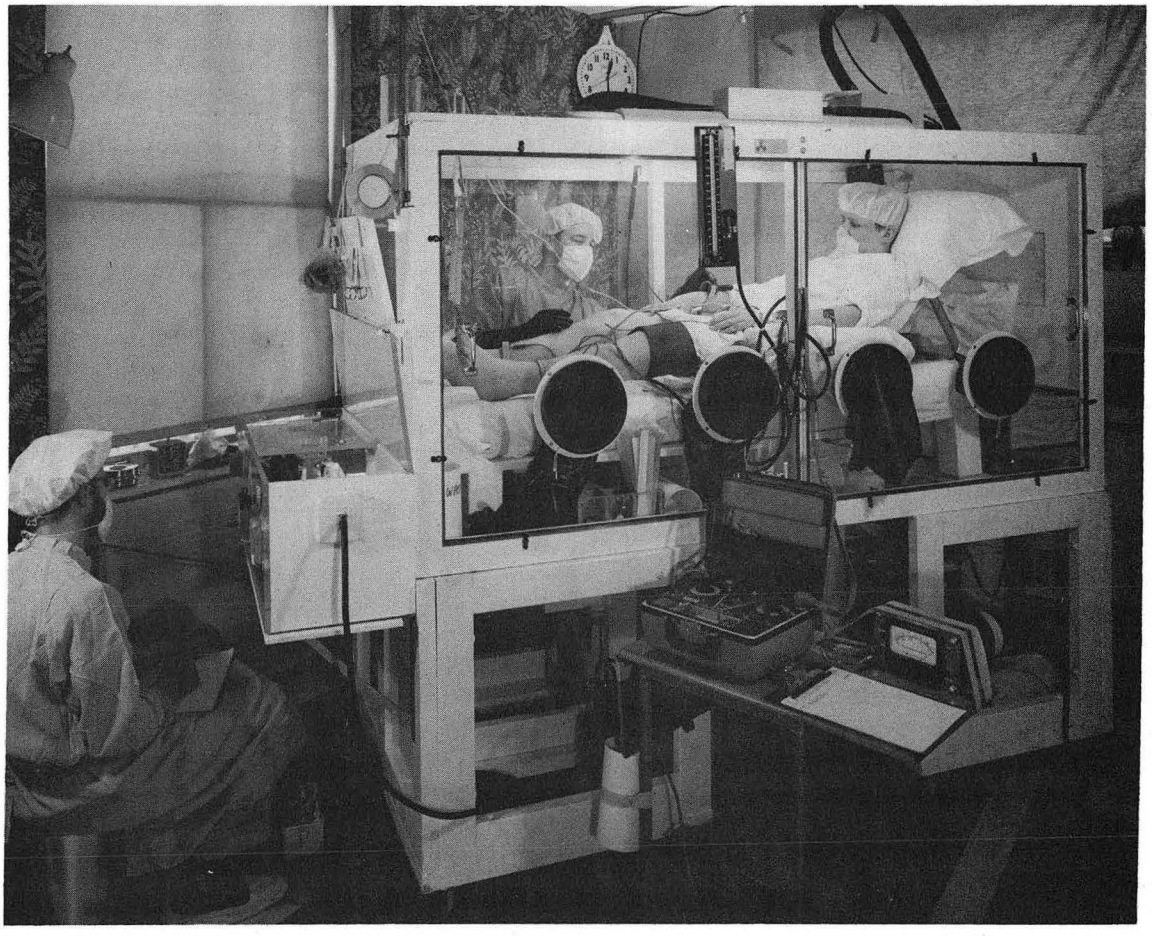
MU-26832

Fig. 9



ZN-3143

Fig. 10



ZN-3136

Fig. 11